Effective Methotrexate Treatment of Polymyositis in an HIV/HCV-Coinfected Patient, Treated with Interferon Alpha 2B

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Presentation:
An HIV/Hep C patient being treated with interferon alpha 2B developed polymyositis and was treated with methotrexate and prednisone over a long period of time.

History:
A 50-year-old Caucasian intravenous drug abuser was first diagnosed with HIV in October of 1994. His CD4 count was 195 cells/µL, and he was started on zidovudine (AZT) monotherapy and sulfamethoxazole/trimethoprim double strength (Bactrim DS). He was then lost to follow up. In February 1996 he moved back to the area on no medications, and presented to clinic with oral thrush. He was started on didanosine (DDI), fluconazole (Diflucan), and Bactrim DS. In June of 1996 his viral load was 200,000 copies/mL, and indinavir (Crixivan) was added to his regimen. In September of 1996 his CD4 count was 24 cells/µL, and lamivudine (3TC), AZT, and rifabutin were added to the regimen. There followed several no-shows to the clinic. In October of 1997 he returned to clinic having stopped all of his mediations in April due to nausea. His HIV viral load was 360,000 copies/mL, CD4 was 47 cells/µL, and he was started on nevirapine (Viramune), stavudine (D4T), lamivudine (3TC), and indinavir, clarithromycin (Biaxin), and Bactrim DS.

In November of 1997 he tested positive for Hepatitis C virus (HCV). His first HCV viral load in March of 1998 was 6,700,000 copies/mL. In April of 1998 he was started on interferon alpha 2B 3 million units IM Monday, Wednesday, and Friday. At this time his HIV viral load was <400 copies/mL, CD4 = 267 cells/µL, and ALT was 114 U/L. In July of 1998, he developed painless proximal muscle weakness. The next month his muscle weakness increased and all medications were stopped. His creatine kinase (CK) was 5,207 U/L, CD4 = 407 cells/µL, and westergren sedimentation rate was 81 mm/hr. By September of 1998 the weakness had increased to the point that he could no longer squat down, and was developing proximal weakness in his arms. He could no longer lift his legs to set his feet on the pegs of his motorcycle. His labs showed an Aldolase = 20.1, ANA <1:40, RF <20, AST = 163 U/L, ALT = 179 U/L. A muscle biopsy of his quadriceps was done (see Pathology pictures).

Physical Exam:
General- White male, thin, weak, unable to stand up with out help.
Mouth-Poor Dental Repair
Neck-No nodes, No JVD, supple
Lungs-Clear to auscultation, no wheezes
Heart-RRR No Murmurs,
Abdomen-Rotund, Non Tender
Extremities: Thin

Differential Diagnosis:
Bohan A. et al lists four criteria to definitively diagnose polymyositis. They are: 1) Proximal muscle weakness, 2) Muscle biopsy showing myositis, 3) Elevated skeletal muscle enzymes, and 4) Electromyographical (EMG) evidence of muscle injury.(1) Our patient had elements of all four criteria, thereby meeting the strict definition of polymyositis.

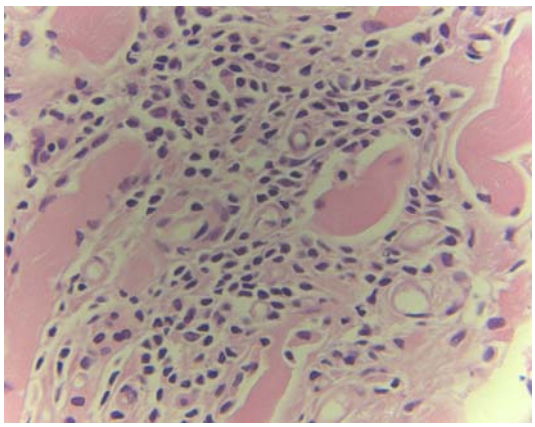
1. Differential Diagnosis: Polymyositis
A. HIV Infection <http://www.fpnotebook.com/HIV11.htm>.(2,3,4) An interesting observation is that the PM started about the time that he had a marked improvement in his HIV status, with a viral load having dropped to below 400 copies/ml and a CD4 of 267 cells/µL. It would be impossible to say at this point how this improvement in HIV status may have triggered the PM if at all.

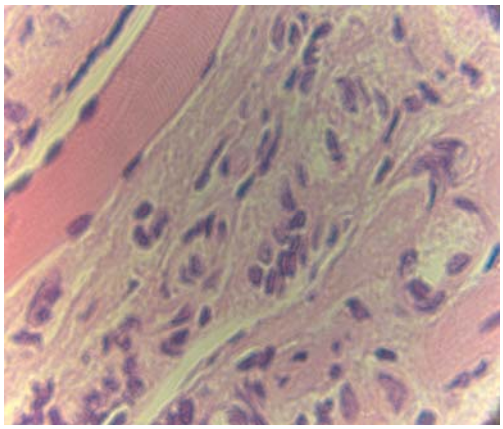
B. Hepatitis C Virus: Ueno Y. et al report of a case of polymyositis in a Hep C patient occurring with chronic hepatitis C virus (HCV) antigenaemia.(5)

C. Zidovudine Therapy: An increasing number of patients receiving long-term zidovudine therapy have had myopathic symptoms such as myalgia (in up to 8 percent of patients), elevated serum creatine kinase levels (in up to 15 percent), and muscle weakness. These symptoms generally improve when zidovudine is discontinued.(6,7) It is unlikely that AZT triggered the PM, because he was only treated with AZT for one month in 1994 and one month in 1995, and two months in 1996, and, finally, 3 months in 1997 (all due to patient's non-compliance). Additionally, the quadriceps muscle biopsy did not show mitochondrial damage.

D. Interferon therapy: Matsuya M. et al reported a single case of polymyositis associated with interferon therapy.(8)

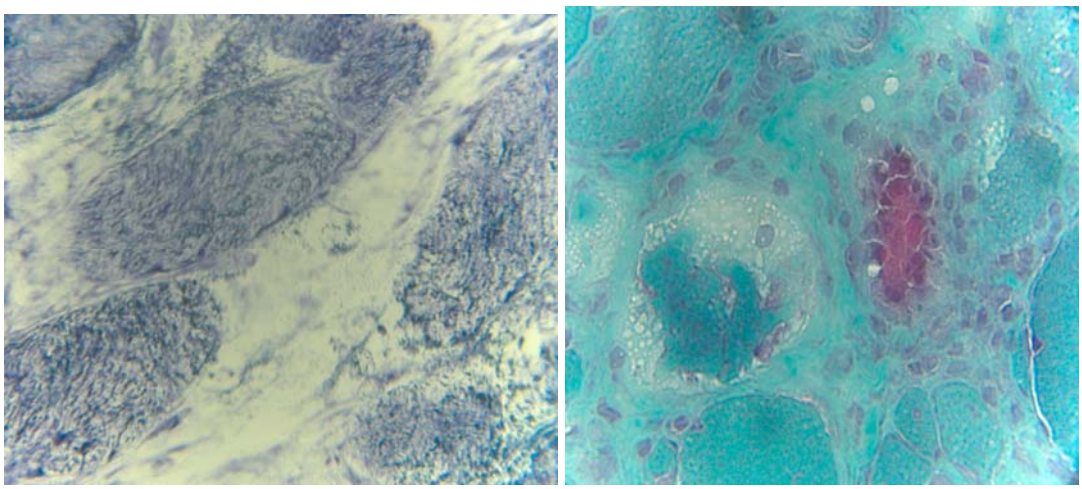
Pathology report:
A muscle biopsy of his quadriceps muscle showed variation in fiber diameter of 5-110 (m, intense endomysial lymphoplasmacytic infiltrate and fibroblastic response, occasional ragged red fibers, and rimmed vacuoles, and myonal necrosis associated with mononuclear infiltration. Stains for acid-fast bacteria, fungi, and toxoplasmosis were negative. SDH staining showed normal mitochondria. See pictures below.





Left panel:
Endomysial lymphoplasmacytic infiltrates

Right panel:
Normal muscle fiber and infiltrates



Left panel:
Normal mitochondria
Right panel: Rimmed Vacuoles

Diagnosis:
Polymyositis most likely caused from interferon therapy.

Discussion:
Regardless of the mechanism triggering the PM in this case, MTX and prednisone were strikingly effective in relieving the patient's weakness and causing biochemical remission. Long-term MTX therapy had no adverse impact on his HIV status. This patient had been off and on antiretrovirals for years before settling into a stable regimen but he was still able to develop immunological and virological recovery.

Clinical course:
In December 1998 the patient was started on Methotrexate (MTX) 50 mg IM weekly, followed by Leucovorin 5 mg PO 24 hours after MTX, Prednisone 30 mg PO QD, and Nevirapine, D4T, 3TC, Crixivan, and Bactrim DS.(9,10,11,12) Within one month his strength had improved and he had noticeably increased muscle bulk. By February 1999 he felt great; his muscle strength continued to improve and his HIV viral load was 684 copies/ml and CD4 count was = 51 cells/μL. His antiretrovirals were changed to efavirenz (Sustiva), nelfinavir (Viracept), 3TC, and D4T. By March prednisone taper had begun, and MTX was increased to 85 mg IM weekly. In April, electromyography (EMG) demonstrated an abundance of small polyphasic units consistent with myopathy. Thereafter he was controlled on maintenance doses of MTX ranging from 37.5-50 mg weekly. He continued to receive MTX weekly and his last CK in January of 2004 was 303 U/L, HIV viral load <50 copies/mL, CD4 = 410 cells/μL, and ALT of 23 U/L. Then in July of 2004 the patient's cat died, and he reported that he had stopped taking his HIV meds and MTX. By October of 2004 his VL was 6686 copies/mL and CD4 = 381 cells/μL. We did not see him until he came to the hospital in March of 2005 with complaints of diarrhea. His stools were positive for cryptosporidium and his CD4 = 53 cells/μL. He declared that he wanted only comfort care measures, and he passed away on 4/21/2005.

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